

Sympathetic Predominance in Young Male White-Collar Workers with Mild to Moderate Hypertension

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Abstract: In order to investigate the difference in diurnal variation of autonomic control between young male mild to moderate hypertensive and normotensive white-collar workers, we assessed heart rate variability with ambulatory blood pressure for over 24 hours including work and sleep periods. Both mean systolic and diastolic blood pressures (SBP and DBP) were significantly ($p < 0.01$) higher in hypertensives (HT, $n = 11$) than normotensives (NT, $n = 11$) in all phases, whereas heart rate was not different between them in any phase. Blood pressures during work period (on-duty) were significantly higher than those during non-work period (off-duty) in both NT and HT. High frequency (HF; 0.15–0.40 Hz) power showed a circadian pattern in phase with the sleep-wake cycle. Both HF and low frequency (LF; 0.05–0.15 Hz) powers in HT were significantly lower than that in NT during the sleep period ($p < 0.05$). LF/HF ratio showed a circadian pattern that was almost opposite of the pattern in HF power. Twenty-four-hour average LF/HF in HT was higher than that in NT ($p < 0.05$). Especially during on-duty, LF/HF in HT was significantly higher than in NT ($p < 0.05$). The increase of SBP and LF/HF from off-duty period to on-duty period (Δ SBP and Δ LF/HF) showed significant positive correlation ($r = 0.67$, $P < 0.05$) in HT group, suggesting that the SBP elevation during on-duty in HT may be coupled with sympathetic activation. These results suggest that HT showed significantly reduced parasympathetic control during sleep and an increased sympathetic activity especially during on-duty as compared with NT. Our findings imply that persistence of sympathodominant states together with reduced vagal activity in young mild to moderate hypertensive workers may be related to future cardiovascular disorders.

Key words: Circadian variation, Autonomic function, Heart rate variability, Hypertension, White-collar worker

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Introduction

Hypertension is one of the major risk factors of ischemic heart disease. Thus far, several mechanisms in the genesis of hypertension have been proposed. In the early phase of young borderline hypertension, sympathetic drive to the heart and blood vessels is increased while parasympathetic tone is decreased¹⁻³, which probably contributes to the progression of cardiovascular diseases. It has been also reported that job strain relates to the elevation of blood pressure⁴ and self-perceived psychological stress is an independent risk factor of coronary artery disease in middle-aged men⁵. Although previous data from controlled laboratory studies showed changes of stress hormones, such as epinephrine and norepinephrine, with many life stressors^{6,7}, there is little data describing the autonomic nervous changes among various active phases in a real life including the work period. Furthermore, the characteristics of autonomic nervous functions have not been reported in young mild to moderate hypertensive workers during various active phases including work and sleep periods. Determining the characteristics of autonomic changes for hypertensive workers is important in order to reduce the detrimental effects of work and/or life stresses on autonomic functions. In this study, we attempted to describe the diurnal variation of autonomic functions and blood pressure in young male white-collar workers with mild to moderate hypertension compared to normotensive workers in a software developing company in Japan.

Materials and Methods

Study subjects

The subjects were 11 mild to moderate hypertensives (HT; mean age 33.4 ± 4.2 yrs, mean blood pressure $150.5 \pm 17.5/94.7 \pm 8.8$ mmHg) without any other medical disorder nor antihypertensive drugs and 11 normotensives (NT; mean age 33.5 ± 4.0 yrs, mean blood pressure $118.5 \pm 9.7/77.7 \pm 7.4$ mmHg) young male white-collar workers. The subjects worked in a data processing and software development company in Tokyo, Japan. All of them were engaged in system engineering and programming, worked from 9:30 to 18:30, and frequently worked overtime until midnight. As cardiac parasympathetic activity indicated by heart rate variability changes with increasing age⁸⁻¹⁰ and obesity¹⁰, we selected the NT and HT subjects matching for age and body mass index (BMI). Subjects were requested to refrain from smoking and drinking alcohol on the experimental day in order to avoid their acute effects on autonomic nervous

function^{11,12}. Informed consent to participation in this study was obtained from each subject.

Blood pressure and heart rate variability measurements

Systolic and diastolic blood pressures (SBP and DBP) were measured with a sphygmomanometer on the right arm in a seated position after a five-minute rest. Two measurements were taken and averaged. All the subjects were classified as HT (mild to moderate hypertension) or NT according to the JNC V (Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure) criteria¹³. Standing height and body weight in clothing were measured. BMI was calculated as weight (kg)/height (m)².

Ambulatory blood pressure and electrocardiograms (ECG) monitoring (TM-2425; A&D Co. Tokyo, Japan) were carried out on a weekday (from Tuesday to Thursday) for over 26 hours for each subject during study periods (from May to July 1997). Blood pressure was measured and recorded every 30 min by the cuff-oscillometric method. R-R interval data for 512 consecutive heartbeats were measured every 30-min as one segment for the same periods as blood pressure measurement. All the recordings started at approximately 8:30, and finished at 10:30 the next day. Data used in the subsequent analysis were started two hours after the beginning of measurements, in order to avoid initial effects of the experimental conditions on BP and heart rate. ECG was recorded on an analyzing processor TM-2425 through an AD-converter at a sampling rate of every 7.8 millisecond. Each R spike was detected with a preset threshold in order to measure R-R intervals. R-R interval power spectra were computed with an analyzing processor TM-2425. Power spectral densities were computed by an autoregressive model and the magnitude of each spectral component was shown as the calculated power, expressed in msec². The low frequency power spectrum (LF; 0.05–0.15 Hz) band reflects both vasomotorial sympathetic and parasympathetic activities modulated by baroreflex sensitivity^{14,15}. The power spectrum band in high frequency (HF; 0.15–0.40 Hz) reflects mainly vagal activity related to respiration^{14,16}. In this study, we adopted HF power as an index of cardiac parasympathetic nervous function, and the ratio of the power spectra in LF and HF (LF/HF) as an index of sympathetic modulations which is considered to be reflective of sympathovagal balance¹⁷.

Blood pressure and autonomic nervous function were calculated as average values during the wake and sleep periods. Wake period was further divided into work (on-duty) and non-work (off-duty) periods. Information about overtime work per month in the last 3 months was also obtained from the subjects.

Statistical analysis

Data are given as the mean ± SD. The significance of differences between NT and HT was tested with unpaired t-test. The significance of difference between different activity phases within group was tested with paired t-test. A probability P<0.05 was taken as significant.

Results

Physical characteristics of the subjects are shown in Table 1. Physical characteristics were not different between the two groups except for blood pressures. The number of current drinkers was higher in HT. Mean working hours and sleep

hours in HT and NT in the experimental day were 11.1 ± 2.0 vs. 11.1 ± 1.6 and 6.2 ± 1.2 vs. 5.8 ± 1.4 hrs, respectively, which showed no difference between the two groups. The amount of overtime worked in the last 3 months in HT was 53.6 ± 30.4 hrs/month, which tended to be longer than that in NT (45.5 ± 25.4 hrs/month), but the difference was not significant.

Diurnal blood pressure changes of both NT and HT showed a circadian pattern following the sleep-wake cycle. SBP, DBP and heart rate (HR) values in the activity and sleep phases are shown in Table 2. Both SBP and DBP were significantly (p<0.01) higher in HT than NT during all phases, whereas HR was not significantly different between the two groups. SBP and DBP during on-duty were significantly higher than those during off-duty both in NT and HT (p<0.05 or p<0.01, respectively).

Figure 1 demonstrates the diurnal changes of HF power assessed by heart rate variability in NT and HT. HF power showed a circadian pattern following sleep-wake cycle. HF power in HT tended to be lower than in NT among various activity phases. Significantly decreased HF power in HT was observed (p<0.05) as compared to NT during the sleep period (Table 3). Diurnal variations of LF power in NT and HT are shown in Fig. 2. LF power also showed a circadian pattern in NT, but such pattern was less evident in HT, resulting in significantly decreased values (p<0.05) in HT during the sleep period (Table 3). Figure 3 illustrates the diurnal changes of LF/HF ratio. The LF/HF showed a

Table 1. Physical characteristics of normotensive (NT) and hypertensive (HT) subjects

	NT	HT
Number (n)	11	11
Age (yrs)	33.5 ± 4.0	33.4 ± 4.2
Height (cm)	168.2 ± 2.2	172.3 ± 5.1
Weight (kg)	70.6 ± 3.2	75.3 ± 5.1
Body mass index (kg/m ²)	24.9 ± 1.3	25.4 ± 1.4
Systolic blood pressure (mmHg)	118.5 ± 9.7	150.5 ± 17.5**
Diastolic blood pressure (mmHg)	77.7 ± 7.4	94.7 ± 8.8**
Smoker/non smoker (n)	4/7	4/7
Drinker/non drinker (n)	6/5	10/1

**P<0.01 vs NT. Values are mean ± SD.

Table 2. Systolic/diastolic blood pressures and heart rate of normotensive (NT) and hypertensive (HT) subjects in the various activity phases

		NT (n=11)	HT (n=11)
24 h	SBP (mmHg)	121.2 ± 5.1	140.1 ± 12.3**
	DBP (mmHg)	74.7 ± 4.8	91.8 ± 8.9**
	HR (beat/min)	71.8 ± 6.9	75.3 ± 7.8
awake	SBP	128.3 ± 5.9	145.4 ± 12.1**
	DBP	80.2 ± 5.0	96.7 ± 8.5**
	HR	77.3 ± 7.9	80.1 ± 8.0
on-duty	SBP	130.2 ± 5.1	146.9 ± 11.4**
	DBP	81.3 ± 5.4	98.7 ± 8.0**
	HR	77.9 ± 8.6	80.3 ± 8.6
off-duty	SBP	124.5 ± 7.7	142.7 ± 14.3**
	DBP	77.8 ± 5.6	93.1 ± 9.9**
	HR	76.5 ± 8.4	80.3 ± 9.2
sleep	SBP	102.8 ± 5.5	124.2 ± 11.5**
	DBP	60.2 ± 6.2	77.4 ± 8.9**
	HR	57.6 ± 7.5	61.8 ± 8.7

**P<0.01 vs NT, # p<0.05, ## p<0.01 between on-duty and off-duty. Values are mean ± SD.

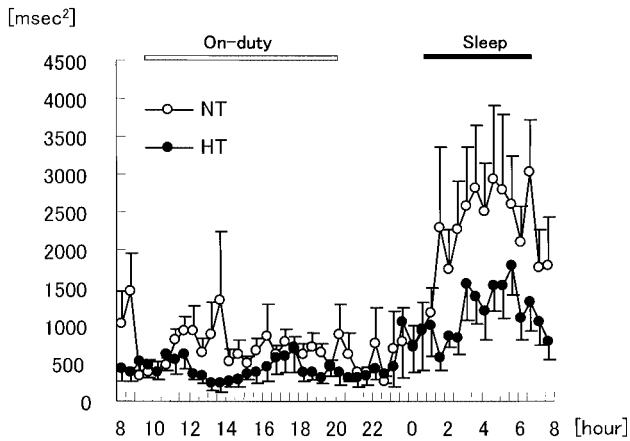


Fig. 1. Circadian variation of high frequency (HF) power (mean \pm SEM) in normotensive () and hypertensive () subjects. Horizontal bars indicate the mean on-duty () and sleep times () of all subjects.

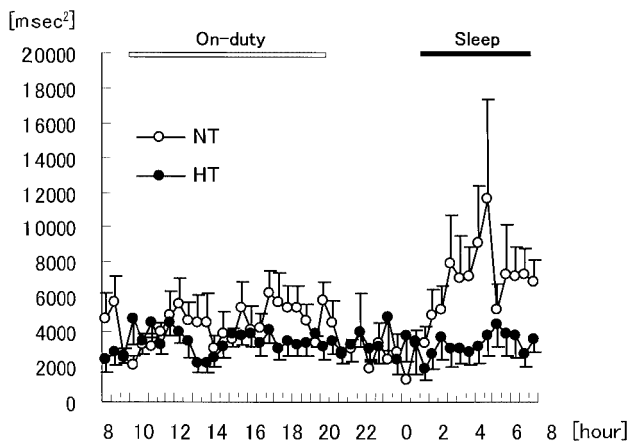


Fig. 2. Circadian variation of low frequency (LF) power (mean \pm SEM) in normotensive () and hypertensive () subjects. Horizontal bars indicate the mean on-duty () and sleep times () of all subjects.

circadian pattern that was almost opposite of the pattern in HF power. Twenty-four-hour average LF/HF in HT was higher ($p < 0.05$) than in NT (Table 3). During work, LF/HF was again significantly higher ($p < 0.05$) in HT as compared with NT. On the other hand, there was no difference between the two groups in HF/LF during off-duty or during the sleep period.

The correlation between the differences of SBP (Δ SBP) between on-duty and off-duty and of LF/HF (Δ LF/HF) in NT and HT are shown in Fig. 4. Significant positive correlation ($r = 0.67$; $p < 0.05$) was observed between Δ SBP and Δ LF/HF only in HT group.

Table 3. Autonomic nervous activities of normotensive (NT) and hypertensive (HT) subjects in the various activity phases

		NT (n=11)	HT (n=11)
24 h	ln (LF)	8.22 \pm 0.55	7.87 \pm 0.66
	ln (HF)	6.65 \pm 0.71	6.01 \pm 0.79
	ln (LF/HF)	1.79 \pm 0.29	2.15 \pm 0.46*
awake	ln (LF)	8.09 \pm 0.59	7.90 \pm 0.65
	ln (HF)	6.17 \pm 0.72	5.60 \pm 0.90
	ln (LF/HF)	2.02 \pm 0.33	2.42 \pm 0.51*
on-duty	ln (LF)	8.18 \pm 0.60	7.97 \pm 0.67
	ln (HF)	6.26 \pm 0.69	5.58 \pm 0.94
	ln (LF/HF)	1.99 \pm 0.31	2.47 \pm 0.53*#
off-duty	ln (LF)	7.83 \pm 0.64	7.71 \pm 0.75
	ln (HF)	5.93 \pm 0.95	5.58 \pm 0.93
	ln (LF/HF)	2.06 \pm 0.41	2.30 \pm 0.50
sleep	ln (LF)	8.53 \pm 0.76	7.74 \pm 0.76*
	ln (HF)	7.54 \pm 0.82	6.86 \pm 0.68*
	ln (LF/HF)	1.01 \pm 0.31	0.99 \pm 0.49

* $p < 0.05$ vs NT, # $p < 0.05$, \$ $p < 0.1$ between on-duty and off-duty. Values are mean \pm SD.

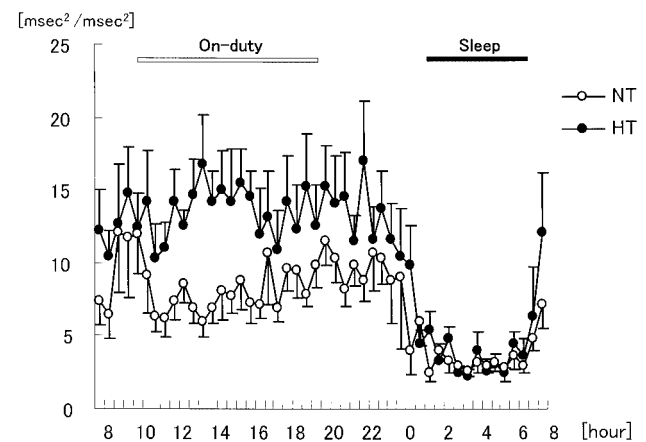


Fig. 3. Circadian variation of LF/HF ratio (mean \pm SEM) in normotensive () and hypertensive () subjects. Horizontal bars indicate the mean on-duty () and sleep times () of all subjects.

Discussion

In this study, we assessed diurnal blood pressure and autonomic nervous changes in young male NT and untreated mild to moderate HT during a typical weekday, including the daily mental and/or physical work stress typical to a working period. We confirmed that diurnal changes of BP and autonomic nervous activities indicated by HF, LF power

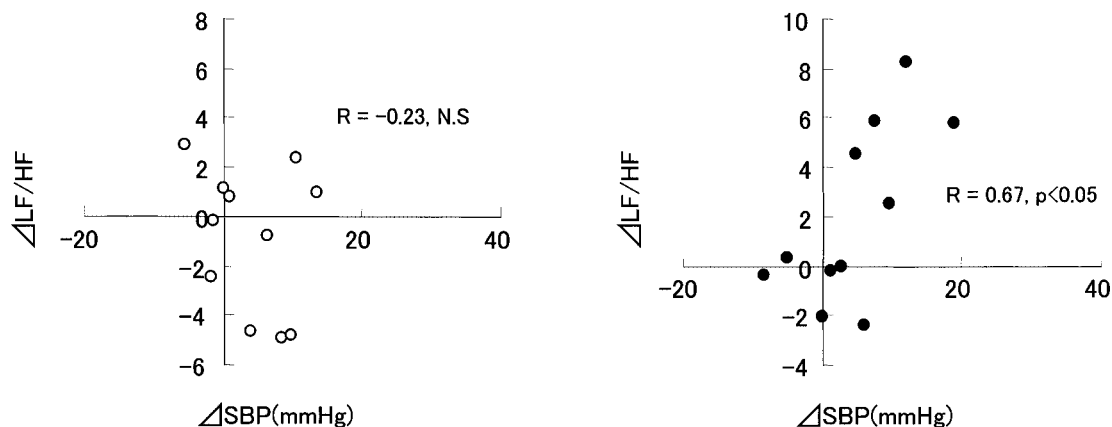


Fig. 4. Relation between ΔSBP and ΔLF/HF in normotensive (○) and hypertensive (●) subjects.
 In hypertensive subjects, ΔLF/HF showed significant positive correlation with ΔSBP. However in normotensive subjects, the relation was not statistically significant.

and LF/HF ratio showed a clear circadian pattern following the sleep-wake cycle in NT. These results are consistent with those of previous reports in normotensive workers¹⁸⁻²⁰. We also found an altered pattern of circadian neural control of heart rate in HT as compared to NT. Using spectral analysis of R-R intervals of heart rate^{14, 21}, enhanced sympathetic activity and reduced vagal activity in essential hypertension compared with normotension was proposed²². An altered pattern of circadian autonomic nervous control between normotension and mild hypertension was recognized by several studies^{23, 24}. Guzzetti *et al.*²³ reported a reduced day-night oscillation in sympathetic activity in essential hypertension as compared with normotension. We also recognized reduced circadian oscillation of autonomic nervous changes in HT as expressed by HF and LF.

Patients with borderline hypertension have a high risk of developing sustained hypertension relative to the normotensive population. It is reported that about 20% of borderline hypertension will develop into a more advanced form of hypertension over 10 years²⁵. In addition, cardiovascular hyperreactivity to mental stress^{26, 27} or physical stress^{28, 29} has been reported to predict the onset of hypertension. The important findings in this study are that cardiac parasympathetic nervous activities were significantly depressed during sleep and sympathetic nervous activities were highly activated during awakefulness, especially during on-duty in HT as compared to NT. Itoh *et al.*³⁰ reported that sympathetic activity assessed by L/H response to mental arithmetic stress was larger in 30-year-old borderline hypertensives than normotensives under laboratory conditions. Our results indicate that sympathetic overactivity in young mild to moderate hypertensives is found especially

during the working period, suggesting that the autonomic nervous response to job stress may function differently in HT and NT.

Moreover, we found a positive correlation between the changes of SBP and LF/HF (ΔSBP and ΔLF/HF) from the off-duty period to the on-duty period, only in HT group. This suggests that elevation of blood pressure during on-duty period might be coupled with enhanced sympathetic activity in the HT group. Our previous study³¹ also revealed the association among self-reported job-stress, sleep quality and daytime autonomic activities in workers employed by the same company of this study. On the other hand, we identified that HF power during on-duty was significantly higher than during off-duty in NT with higher BP during on-duty compared to off-duty (Table 3). The reason of this inconsistent result is not clear. One possibility is that regulation of BP during on-duty may not predominantly depend on parasympathetic regulation. All of our subjects were white-collar workers, system engineers, who engaged in data processing and software development mainly in a sitting position. Therefore, posture and physical activity which would affect autonomic nervous function were not different between HT and NT during on-duty.

During the sleep period, we confirmed significantly reduced parasympathetic tone without changing sympathovagal balance in HT as compared with NT. Reduced HF power during sleep in HT compared to NT was also recognized in some studies^{23, 24}. It was reported that reduced heart rate variability (reduced HF components) and baroreflex sensitivity were closely related to cardiac sudden death^{32, 33}. Our findings of more reduced HF power in HT as compared with NT during sleep period implies increased cardiovascular

risks in HT. In the present study, we did not obtain the data of sleep stages, which would affect cardiac autonomic control differently^{34,35}. But since the sleep structures have also been reported to be similar between NT and HT³⁶, it seems unlikely that the observed difference in autonomic control between NT and HT during sleep was not ascribed to the effects of sleep structures.

In conclusion, we confirmed in this study that diurnal changes of autonomic nervous activities showed altered pattern between NT and HT young male white-collar workers. We also recognized that young mild to moderate HT showed significantly reduced parasympathetic control compared to NT during sleep and that HT showed a sympathodominant state, especially during the on-duty period. These results imply that persistence of the sympathodominant state together with reduced vagal activity in young HT may be related to the progression of future cardiovascular disorders. Our findings presented in this study may be of help for improvement of work conditions, especially for mild to moderate hypertensive workers. Also, it will be necessary to conduct follow up study of these subjects in order to reveal more a detailed relationship between autonomic nervous and blood pressure profiles.

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